US Army Medical Research and Materiel

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Method of Diagnosing Exposure to Toxic Agents By Measuring Distinct Pattern In the Levels of Expression of Specific Genes

Features and advantages:

- **Significant alterations in host gene expression allow biological threat agents to be discriminated**
- **Alterations were shown using human lymphocytes *in vitro***
- **Have amplified, sequenced, and identified a few hundred genes using differential display**
- **Findings have been verified in lymphocytes of challenged with SEB**
- **Unique gene found within 30 minutes of post-aerosol SEB and 24 hours of post-aerosol anthrax challenge of monkeys**

This invention provides a method of diagnosing the exposure of a subject to biological threat agents based on relative ratios, amounts of changes in levels of the genes and/or proteins in mammalian tissues or body fluids as compared to levels in normal, unexposed tissues or fluids. A determination of the difference in the detected amount of protein/gene expression between the exposed and unexposed samples can be made and compared to a library of expected expression levels for predetermined toxic agents.

Counter-terrorist efforts have been aimed at rapid, accurate diagnosis of infectious agents followed by speedy treatment to prevent irreparable damage, incapacity, and death. Identification of toxic agents has previously been based on their structural characteristics. This invention relies on individual host responses and is independent of the need to determine which toxic agent is present. The type of impending illness (shock, neurological toxicity, etc) could be determined by analyzing gene expression patterns of the peripheral blood lymphoid cells from exposed individuals. Human lymphocytes and monocytes from healthy human donors were obtained and exposed to various toxins, including staphylococcal enterotoxin B (SEB), anthrax, *Yersinia pestis* (plague), and cholera toxin and alterations in gene expressions noted. These gene expression patterns can discriminate one agent from the other.

When monkeys were challenged with SEB or anthrax, the selected genes were altered as predicted in response to SEB. The genes not only provide diagnostic capabilities for toxic agents but also indicate exposure dose and provide potential new targets for events that ultimately lead to lethal shock.

Patent Status

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KEYWORDS: Host gene responses; diagnostic assay; gene profiles; biological threat agents; lymphoid cells; gene array; differential display

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